Docket No.: 649218007US
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Michael D. Laufer

Application No.: 09/095,323 | Confirmation No.: 9521

Filed: June 10, 1998 | Art Unit: 3769

For: METHOD AND APPARATUS FOR TREATING SMOOTH MUSCLES IN THE WALLS OF BODY CONDUITS | Examiner: D. M. Shay

REPLY BRIEF UNDER 37 C.F.R. § 41.41

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The present communication responds to the Examiner's Answer dated June 13, 2011 in the above-identified application. In the Examiner's Answer, the Examiner attempted to address the bases for overcoming the rejections established by the Appellants in the Appeal Brief filed August 13, 2009. However, the Examiner's rationale is flawed at least for the reasons explained in detail below.

The Appellant thanks the Examiner for withdrawing the following rejections: claim 55 under §112, second paragraph; claims 30, 32, 33, 35, 37, 52, 53, 56, 58 and 59 under §102 over Ivanyuta; and claims 29, 30, 32-35, 37, 50 and 52-59 under the doctrine of obviousness-type double patenting over U.S. Patent No. 6,488,739 and/or U.S. Patent Application No. 11/408,668. The rejections maintained by the Examiner are as follows:

(A) claims 29-37, 50 and 52-62 under §112, first paragraph;

(B) claims 29-37, 50 and 52-62 under §112, second paragraph;

(C) claims 29, 32-34, 36, 37, 50 and 56-59 under §103 over the combination of James, Clarke, Waksman and Regunathan;

(D) claims 30 and 35 under §103 over the combination of James, Clarke, Waksman, Regunathan and Vincent;

(E) claims 52-55 under §103 over the combination of James, Clarke, Waksman, Regunathan and Lax;

(F) claims 60-62 under §103 over the combination of James, Clarke, Waksman, Regunathan, Robinson and Levenson; and

(G) several provisional obviousness-type double patenting rejections.

The Examiner's Answer mailed on June 13, 2011, includes several assertions regarding the Appellant's arguments, the meaning of the cited references, the understanding of a person of ordinary skill in the art, and the evidentiary weight given to the Declaration of Dr. Michael Laufer Under 37 C.F.R. § 1.132 (the "Laufer Declaration"). In this paper, the Appellant addresses several, but not all of the errors in Examiner's Answer in the interest of brevity and clarity. More specifically, the Appellant addresses portions of rejections (A)-(C) set forth above, and the errors noted below regarding rejection (C) also apply to rejections (D)-(F). The Appellant maintains the errors explained in the Appeal Brief and respectfully does not concede the Examiner's assertions in the Examiner's Answer.

A. Reply Regarding Rejection Under Section 112, First Paragraph

The Appellant respectfully submits that the basis articulated in the Examiner's Answer for the §112, first paragraph, rejection is incorrect for several reasons. Claim 50 was initially rejected under §112, first paragraph, on the grounds that the originally filed specification did not reasonably convey to one skilled in the art that the inventors had possession of a treatment including irradiating the airway wall to cause debulking of the airway smooth muscle "such that the ability of the smooth muscle to contract is reduced." (See, e.g., the Final Office Action dated April 4, 2008.) At that time, the Examiner asserted that the specification supported reducing or debulking of the airway

smooth muscle, but did not expressly support that the reduction of the smooth muscle tissue is the same as a reduction in the ability of the smooth muscle to contract. The Appellant discussed this rejection with the Examiner during the personal interview on June 28, 2008, and the Examiner agreed that the phrase "such that the ability of the airway to contract is reduced" was supported by the originally filed specification. For example, page 11, lines 5-9, of the originally filed specification reads "The elimination of smooth muscle tissue prevents the hyperactive airways of an asthma patient from contracting or spasming, completely eliminating this asthma symptom." This portion of the originally filed specification expressly and unambiguously establishes that the treatment possessed by the inventor at the time of the invention irradiated the wall of an airway of an asthmatic lung and eliminated smooth muscle tissue such that the ability of the airway to contract is reduced. Therefore, this rejection should be withdrawn.

The Examiner now contends that the present claim language does not comply with the requirements of §112, first paragraph, on the grounds that there is no disclosure of any particular parameters with regard to power, power density, or energy density, for example, that would produce this particular result. It appears that the Examiner is transitioning this rejection from whether the claimed subject matter is supported to whether the specification provides an enabling disclosure commensurate with the scope of the claimed subject matter. A claim complies with the enablement aspect of §112, first paragraph, if a person skilled in the art can make and use the invention without undue experimentation. (MPEP §2164.01.) The fact that experimentation may be complex does not necessarily make it undue when the art typically engages in such experimentation. (Id.)

The originally filed specification provides sufficient disclosure to enable a person skilled in the art to practice the scope of claim 50 without undue experimentation because it teaches particular types of energies (e.g., wavelengths of light) and the parameters for determining the intensity of the light. For example, the originally filed specification states:

> The energy used may be coherent or incoherent light in the range of infrared, visible, or ultraviolet...Preferably the light is ultraviolet light having a wavelength of about 240-280 nm or visible light in the red visible range.

> The intensity of the light may vary depending upon the application. The light intensity should be bright enough to penetrate any mucus present in the airway and penetrate the smooth muscle cells and mucus gland cells to cause cross linking of the cell DNA. The light intensity may vary depending on the wavelength used, the application, the thickness of smooth muscle, and other factors. (Specification at page 7, lines 12-22.)

A person skilled in the art could determine the intensity of the light without undue experimentation based, for example, on the statement that the light intensity "should be bright enough to penetrate any mucus present in the airway and penetrate the smooth muscle cells and mucus gland cells to cause cross linking of the cell DNA." The level experimentation is further guided by the teaching that the light intensity may vary depending on the wavelength and thickness of smooth muscle. Therefore, given this roadmap and the sophistication of experiments for developing medical devices, the specification meets the requirements of §112, first paragraph.

B. Reply Regarding Rejection Under Section 112, Second Paragraph

The Appellant respectfully submits that the basis articulated in the Examiner's Answer for rejecting the claims under §112, second paragraph, is also incorrect for the reasons explained above with respect to the §112, first paragraph, rejection. More specifically, claim 50 includes "irradiating walls of an airway of an asthmatic lung...at a wavelength and intensity which, over time, causes debulking of smooth muscle tissue...such that the ability of the airway to contract is reduced." The metes and bounds of claim 50 are sufficient to meet the requirements of §112, second paragraph, for at least the reason that a person skilled in the art could assess the extent of debulking of the smooth muscle tissue and airway contraction. Claim 50, therefore, does not need to recite specific ranges of wavelengths or intensities to provide the public adequate notice of the scope of the claimed subject matter.

C. Reply Regarding Rejection Under Section 103 over James, Clarke, Regunathan and Waksman

The Examiner's rationale set forth in the Examiner's Answer for maintaining the outstanding Section 103 rejection is summarized as follows: (1) James teaches that hypertrophy and hyperplasia of smooth muscle are involved in airway narrowing in asthma (Examiner's Answer at 32); (2) James teaches that the thickening of smooth muscle is due to hyperplasia rather than hypertrophy (Examiner's Answer at 32); (3) James in combination with the knowledge of a person of ordinary skill in the art suggests that symptoms of asthma would be mitigated by reversing smooth muscle hyperplasia (Examiner's Answer at 35); (4) Waksman teaches hyperproliferation of smooth muscle cells causes lumen narrowing, such hyperproliferation of smooth muscle cells can be treated by radiation, and that Waksman's treatment can be employed in the bronchi (Examiner's Answer at 33); (5) Regunathan teaches that a person of ordinary skill in the art would understand that hyperplasia can be termed hypertrophy (Examiner's Answer at 32); (6) hyperplasia and hypertrophy are overlapping with hyperplasia being a subset of hypertrophy (Examiner's Answer at 29-30); (7) Clarke teaches that UV radiation in the 240-280 nanometer range kills vascular smooth muscle cells which would otherwise proliferate (e.g., hyperplasia) and contribute to localized restenosis (Examiner's Answer at 32-33); and (8) a person of ordinary skill in the art would have employed UV radiation in the range of 240-280 nanometers to treat smooth muscle hyperplasia in an asthmatic lung for the reasons stated in points (1)-(7) above.

The Appellant respectfully disagrees with the Examiner's assertions and conclusions. As explained in detail below, the Examiner's Answer includes at least the following error:

> A person of ordinary skill in the art would not use Clarke's method to irradiate airway walls of an asthmatic lung in a manner that causes debulking of the airway smooth muscle and reduces the ability of the airway to contract because unbiased experts at the USFDA believed that decreasing airway smooth muscle mass (i.e., debulking) in only one of five

> lobes of a human lung could lead to complications that outweighed the potential benefits.

The Examiner's grounds for combining James, Clarke, Waksman and Regunathan as set forth in the Examiner's Answer and summarized above are flawed for several reasons. First, the Appellant respectfully submits that the Examiner erred by concluding that the teachings of James "in combination with the knowledge of one of ordinary skill in the art" suggests that the symptoms of asthma would be mitigated by reversing the smooth muscle hyperplasia in the face of expert evidence to the contrary. (Examiner's Answer at 35.) More specifically, based on James's statements that hyperplasia is one of several mechanisms that cause thickening of airway smooth muscle, and even acknowledging that James does not teach any mechanism to debulk airway smooth muscle, it is the Examiner's view that a person of ordinary skill in the art would in fact have considered reducing smooth muscle hyperplasia in an asthmatic lung a viable treatment at the time of the invention. (Examiner's Answer at 35.) However, in contrast to the Examiner's position, the USFDA disapproved the Appellant's application for an investigational device exemption to study treating asthma by decreasing the thickness of the airway smooth muscle (i.e., debulking) and reducing the ability of the airway to contract based on data from a study in which a single lobe in the lung of eight patients was treated. (USFDA Letter regarding IDE No. G010016 at page 1.) Unlike the Examiner, the experts at the USFDA believed that the Appellant's proposed treatment of decreasing airway smooth muscle posed "significant potential risks that appear to outweigh the potential benefits." (USFDA Letter at page 1.) More specifically, the FDA stated:

> Even if normal healing of a larger treated bronchi were to occur, there are significant concerns that the underlying conditions (asthma) would nonetheless remain. Airway smooth muscle facilitates airway dilation as well as airway constriction. Of concern is that ablation of airway smooth muscle and small bronchi may have negative effects by preventing airway dilation during sympathetic stimulation (e.g., during exercise). Patients could conceivably continue to have asthma attacks with secretions and smaller airway bronchospasm and then be unable to effectively cough and

> clear these secretions due to lack of larger airway smooth muscle tone. Reduced smooth muscle support of the conducting airways, coupled with underlying asthma, could lead to complications such as bronchiectasis.

The USFDA accordingly stated that ablation of airway smooth muscle was thought to be too uncertain to approve an investigational device exemption for an in-human trial based on data that involved single-lobe treatments. The Appellant respectfully submits that the USFDA, not the Examiner, possessed the knowledge of one of ordinary skill in the art at the time of the invention. Thus, since the U.S. Government's leading agency for studying the safety and efficacy of medical devices held that a person skilled in the art at the time of the invention would have considered the risks of a procedure to reduce the thickness of existing airway smooth muscle (i.e., debulking) in one lobe of the lung to outweigh the benefits, and since the Examiner uses the "knowledge of one of ordinary skill in the art" to fill in the gaps of James, it follows that the Examiner erred in concluding "the symptoms of asthma would be mitigated by reversing smooth muscle hyperplasia" based on James in combination with the knowledge of a person skilled in the art. This error alone is sufficient grounds to reverse the current rejection based on James, Clarke, Waksman and Regunathan because James is the only reference that the Examiner relies on to suggest that the thickness of airway smooth muscle should be decreased.

The Examiner attempts to overcome the USFDA's undisputed position that, at the time of the invention, the risks of reducing airway smooth muscle for treating asthma outweighed the potential benefits on the grounds that the assertions by the USFDA are not commensurate with the scope of the claims. More specifically, with reference to the USFDA Letter and the Macklin article discussed in paragraph 8 of the Laufer Declaration, the Examiner states these references refer to "total eradication" of airway smooth muscle, and thus are not commensurate with the scope of the claims. (Examiner's Answer at 35-36.) To drive this point home, the Examiner further states:

> The letter from the USFDA indicates that the procedure reviewed entailed <u>total ablation</u> of the smooth muscle <u>throughout the entire airway</u>, rather than any partial ablation, either in thickness or in extent of the airway system, these

> assertions are ... much narrower than the claims that bar.
> (Examiner's Answer at 36, emphasis added.)

The Examiner is simply incorrect. The USFDA Letter clearly states that the data it analyzed was based on treating "one lobe" in the lungs of eight patients. A person skilled in the art would know that the human lung has five lobes. Thus, the USFDA was not analyzing a procedure that entailed "total eradication of the airway smooth muscle," or "total ablation of the smooth muscle throughout the entire airway system" as asserted by the Examiner. Claim 50, moreover, is a "method of treating asthma," which inherently includes debulking the airway smooth muscle such that the ability of the airway to contract is reduced in a sufficient portion of an asthmatic lung to the extent that the asthma symptoms are relieved. The statement by the USFDA denying the Appellant's application for an investigational device exemption is clearly not limited to only a narrow part of the scope of the claims because a person skilled in the art would understand that the USFDA was studying the effect of reducing the thickness of airway smooth muscle (i.e., debulking) in a portion of the lung to the extent necessary to treat asthma. The statement by the USFDA is also directly on point regarding the Examiner's use of the "knowledge of a person of ordinary skill in the art" in combination with James because the USFDA embodies that knowledge. Therefore, the Examiner's primary basis for substituting his judgment for that of the USFDA is directly controverted by the statements in the USFDA Letter.

The Examiner also erred in combining James, Clarke, Waksman and Regunathan on the grounds that treating hyperplasia is tantamount to reducing the thickness of airway smooth muscle based on the flawed rationale that hyperplasia describes a subset of the conditions that are covered by hypertrophy. The Examiner states "hypertrophy can include hyperplasia" to mean that the two terms are "clearly overlapping with hyperplasia describing a subset of the conditions that are covered by hypertrophy." (Examiner's Answer at 29-30.) The Examiner cites Stedman's Medical Dictionary, 26th Edition, stating that the definition of hyperplasia includes "SYN numerical hypertrophy, quantitative hypertrophy" as further evidence that the term hyperplasia is encompassed by hypertrophy. This is incorrect. The primary definition of

hypertrophy is an enlargement of an organ or tissue as a result of an increase in size, while the definition of hyperplasia is the enlargement of a bodily organ or part resulting from an increase in the total number of cells. (Stedman's Dictionary, 26th Edition) Under these definitions, hyperplasia and hypertrophy are mutually exclusive mechanisms of growth. For example, reversing hyperplasia merely results in the prevention of the growth of additional cells that can cause the smooth muscle to become thicker, whereas reversing hypertrophy reduces the thickness of existing smooth muscle mass. Stopping hyperplasia does not necessarily reduce the thickness of existing smooth muscle mass. Therefore, in contrast to the Examiner's position that hyperplasia is encompassed by hypertrophy, these are two different mechanisms of action that result in two different endpoints when they are treated. The Appellant respectfully submits that the rejection of claim 50 over the combination of James, Clarke, Waksman and Regunathan is also improper because the Examiner incorrectly concluded that the art directed to treating the proliferation of new cells (e.g., hyperplasia) is equivalent to the claimed process of treating hypertrophied airway smooth muscle in a manner that reduces the thickness of the smooth muscle.

Accordingly, for at least the foregoing reasons, and those set forth in the Appeal Brief, the Appellant respectfully requests that the Board reverse the rejections of the pending claims.

Respectfully submitted,
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